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## Lentiviral gene therapy for X-linked chronic granulomatous disease.

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### Public Summary:

A clinical trial of gene therapy for X-Linked Chronic Granulomatous Disease (X-CGD) is reported. 7 of 9 treated patients had sustained engraftment of gene corrected stem cells, leading to the production of functional neutrophils and absence of subsequent infections.

### Scientific Abstract:

Chronic granulomatous disease (CGD) is a rare inherited disorder of phagocytic cells<sup>(1,2)</sup>. We report the initial results of nine severely affected X-linked CGD (X-CGD) patients who received ex vivo autologous CD34(+) hematopoietic stem and progenitor cell-based lentiviral gene therapy following myeloablative conditioning in first-in-human studies (trial registry nos. NCT02234934 and NCT01855685). The primary objectives were to assess the safety and evaluate the efficacy and stability of biochemical and functional reconstitution in the progeny of engrafted cells at 12 months. The secondary objectives included the evaluation of augmented immunity against bacterial and fungal infection, as well as assessment of hematopoietic stem cell transduction and engraftment. Two enrolled patients died within 3 months of treatment from pre-existing comorbidities. At 12 months, six of the seven surviving patients demonstrated stable vector copy numbers (0.4-1.8 copies per neutrophil) and the persistence of 16-46% oxidase-positive neutrophils. There was no molecular evidence of either clonal dysregulation or transgene silencing. Surviving patients have had no new CGD-related infections, and six have been able to discontinue CGD-related antibiotic prophylaxis. The primary objective was met in six of the nine patients at 12 months follow-up, suggesting that autologous gene therapy is a promising approach for CGD patients.

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